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Aortic Valve Replacement and Combined Aortic Valve Replacement and Coronary Artery Bypass Grafting: Predicting High Risk Groups

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To determine which groups of patients are at highest risk for operative or late mortality, 259 consecutive patients who underwent operation between 1978 and 1984 were studied; 170 underwent aortic valve replacement and 89 underwent aortic valve replacement combined with coronary artery bypass grafting. Multivariate analysis of risk factors selected emergency operation and patient age older than 70 years as the strongest predictors for operative death. Although patients having aortic valve replacement and coronary artery bypass grafting had a higher operative mortality rate (13.5 versus 3.5%), the combined operation had no independent predictive effect on early or late results.

At a mean follow-up time of 48 months after surgery, 72% of the survivors of operation were living, 10% were lost to follow-up and 18% were dead. Seventy-seven percent of long-term survivors were in New York Heart Association functional class I or II. The incidence of thromboembolism, paravalvular leak, bacterial endocarditis and hemorrhage each occurred at a rate of less than 1% per patient-year. The factors associated with late death were preoperative age, male sex, left ventricular end-diastolic pressure, cardiac index and functional class. Despite an increase in operative mortality, patients undergoing emergency operation were not at higher risk of late death.

Operative mortality is concentrated among several high risk groups. For patients undergoing elective operation, operative mortality is low, especially if the patient is less than 70 years old. Late results are good for all groups of patients undergoing operation, including those who are at greater risk of dying at operation.

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With improvements in myocardial preservation, operative techniques and postoperative care, operative mortality for aortic valve replacement is said to be approximately 5% (1). However, the most recent reports review data on patients operated on between the late 1960s and the early 1980s. These include many patients operated on when operative mortality was higher than it is now (1–4). In addition, these papers deal only with elective operations and do not specifically discuss early and late results for emergency operation.

It is our impression that, when modern techniques are used, the majority of deaths occur in certain high risk groups and that for most patients operative risk is considerably less than 5%. To determine which patients are at high risk for operative and late mortality, and to determine early and late results for emergency as well as elective operations, we have reviewed our experience between 1978 and 1984 with aortic valve replacement and aortic valve replacement combined with coronary artery bypass grafting at this medical center.

Methods

Patient data. This study reviews only data from patients who had aortic valve replacement alone or in combination with coronary artery bypass grafting. Patients having mitral or tricuspid valve replacement as well and those having an operation on the aortic arch in conjunction with aortic valve replacement were excluded. Patients who were less than 18 years old at the time of operation were also excluded. A total of 259 patients were studied; 209 (81%) had an elective operation, and 50 (19%) had an emergency operation. An operation was considered an emergency if it was performed

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Table 1. Results of 50 Emergency Operations

Indication	No.	Operative Mortality Rate	Late Mortality Rate
Unstable angina	19	5 (26.3%)	3 (21.4%)
Rapidly progressive congestive heart failure	15	2 (13.3%)	2 (15.4%)
Bacterial endocarditis	8	1 (12.5%)	0 (0%)
Cardiac arrest in the catheterization lab	4	2 (50%)	0 (0%)
Cardiogenic shock from tachyarrhythmias	4	0 (0%)	0 (0%)
	50	10 (20%)	5 (12.5%)

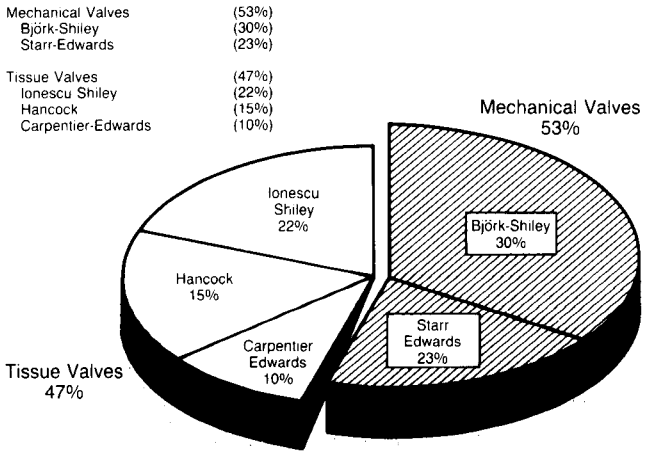
for unstable angina, acute bacterial endocarditis, cardiogenic shock or rapidly progressive congestive heart failure that required stabilization in the intensive care unit (Table 1).

The 259 patients were grouped according to the type of operation required; 170 had aortic valve replacement alone and 89 had aortic valve replacement combined with coronary artery bypass grafting. In the group with valve replacement only, 87 patients had aortic stenosis, 49 had aortic regurgitation and 34 had mixed stenosis and regurgitation. In the group having the combined operation, 64 had aortic stenosis and 25 had aortic regurgitation.

There were 182 men and 77 women in the total study group, aged 18 to 86 years (mean 58). Patients having only aortic valve replacement were younger (range 18 to 83 years; mean 56) than those having a combined operation (range 38 to 86 years; mean 67). Grouped by the New York Heart Association functional classification, 29 (11%) of the 259 patients were in class II, 169 (65%) were in class III and 61 (24%) were in class IV. The types of valves used are illustrated in Figure 1.

Preoperative cardiac catheterization and coronary arteriography were performed on all patients, and coronary artery bypass grafting was performed for all angiographically significant lesions (more than 70% luminal narrowing). The hemodynamic and clinical data are presented in Table 2.

Figure 1. Types of valves used in 259 patients.



Technical details. Cardiopulmonary bypass was performed using a roller pump, bubble oxygenator and moderate systemic hypothermia (25°C) in each case. Topical hypothermia in conjunction with multidose, crystalloid cardioplegia solution provided myocardial protection. It was infused through the aortic root in patients with aortic stenosis and was put directly into the coronary ostia in patients with aortic regurgitation. Both during and after operation, a Swan-Ganz catheter was used for monitoring filling pressures and performing thermodilution cardiac output determinations. Anticoagulant therapy with warfarin was started after the chest tubes were removed, usually on the third postoperative day. All patients with a mechanical valve received warfarin. For patients with a bioprosthesis, warfarin was initially given but was discontinued after 3 months if no thromboembolic events had occurred.

Follow-up. Long-term follow-up reports were obtained for 218 (90%) of the 241 operative survivors. Information was obtained from charts and interviews; many of these patients continue to be seen at our medical center. The remainder of the group was contacted by telephone and

Table 2. Preoperative Clinical and Hemodynamic Data

No. patients	259
Male	182
Female	77
Elective operation	209
Emergency operation	50
AVR	170
AS	87
AR	49
AS and AR	34
AVR and CABG	89
AS and CAD	64
AR and CAD	25
NYHA functional class	
II	29
III	169
IV	61
Hemodynamic data*	
LVEDP (mm Hg)	21.9 ± 11.8
CI (liters/min per m^2)	2.6 ± 0.7
PCW (mm Hg)	16.4 ± 8.1
PAM (mm Hg)	25.1 ± 10.1
Age (yr)	
≤50	48
50–70	158
≥70	53

*Mean and standard deviation. AVR = aortic valve replacement; AS = aortic stenosis; AR = aortic regurgitation; CABG = coronary artery bypass grafting; CAD = coronary artery disease; CI = cardiac index; NYHA = New York Heart Association; LVEDP = left ventricular end-diastolic pressure; PCW = pulmonary capillary wedge pressure; PAM = pulmonary artery mean pressure.

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specifically questioned with regard to exercise tolerance, medications and complications such as stroke, peripheral embolism, hemorrhage, valve failure, endocarditis and reoperation.

Statistical methods: univariate analysis. Actuarial life table analysis, using a generalized Savage test (BMDP-P1L, BMDP statistical software), compared the early and late survivorship of patients having isolated aortic valve replacement and those having combined valve replacement and bypass grafting. The clinical factors evaluated were age, sex, New York Heart Association functional class, emergency or elective operation, mechanical or bioprosthetic valve and type of aortic valve lesion. The hemodynamic factors analyzed were left ventricular end-diastolic pressure, pulmonary capillary wedge pressure, cardiac index and mean pulmonary artery pressure.

Statistical analysis: multivariate analysis. Multivariate analysis using a stepwise logistic regression procedure (BMDP-LR, BMDP statistical software), was applied to the entire study group to identify which factors had the greatest independent effect on operative mortality. Variables included in the analysis were the same as those used in the univariate analysis. After excluding patients who had emergency surgery, the logistic regression analysis was repeated to determine which factors affected operative mortality in the group having elective operations.

The variables that affected long-term survival were analyzed with a stepwise Cox regression procedure (BMDP-2L, BMDP statistical software). This method was employed in addition to the stepwise logistic regression analysis because it models a relative hazard function by incorporating factors that influence survival time throughout the follow-up period. In contrast, the logistic regression procedure models the odds of surviving for a fixed length of time after operation; it does not distinguish between survival times, except to indicate whether or not they exceed the duration of interest.

Results

Operative mortality (Tables 3 and 4). Operative mortality rate was 6.9% (18 of 259). Most of the deaths were secondary to low cardiac output or perioperative myocardial infarction. For the 209 elective operations, there were 8 deaths (3.8%), but for the 50 emergency operations there were 10 deaths (20%). The mortality rate was 16.9% for patients older than 70 years and it was 4.4% for those younger than 70 years. There was no significant difference in mortality rate for aortic stenosis (4.6%), aortic regurgitation (2.0%) or mixed stenosis and regurgitation (2.9%). For isolated aortic valve replacement, the overall mortality rate was 3.5%, whereas for the combined operation the mortality rate was 13.5%.

Table 3. Causes of Operative Death in 18 Cases

Low cardiac output	9
Perioperative myocardial infarction	3
Aortic dissection	2
Respiratory failure	2
Ventricular arrhythmia	1
Aortic perforation from insertion of intraaortic balloon pump	1
	18

Table 4. Operative Mortality by Subgroup

	Deaths	Percent
Overall	18/259	6.7
AVR	6/170	3.5
Elective AVR	2/135	1.5
< 70 yr	1/118	0.8
≥ 70 yr	1/17	5.9
Emergency AVR	4/35	11.4
< 70 yr	4/29	13.8
≥ 70 yr	0/6	0
AVR with CABG	12/89	13.5
Elective	6/74	8.1
< 70 yr	3/53	5.7
≥ 70 yr	3/21	14.3
Emergency	6/15	40.0
< 70 yr	1/6	16.7
≥ 70 yr	5/9	55.6
AS	4/87	4.6
AR	1/49	2.0
AS and AR	1/34	2.9
AS with CAD	9/64	14.1
AR with CAD	3/25	12.0

AR = aortic regurgitation; AS = aortic stenosis; AVR = aortic valve replacement; CABG = coronary artery bypass grafting; CAD = coronary artery disease.

Predictors of operative mortality. Univariate analysis using a generalized Savage test identified the factors most likely to be associated with operative death. Early mortality was different for the combined operation than it was for isolated aortic valve replacement; therefore, the two groups were analyzed separately. In the combined operation group, the chance of operative death increased when the patient was more than 70 years old, the operation was an emergency, the pulmonary capillary wedge pressure was greater than 18 mm Hg, the cardiac index was less than 2 liters/min per m^2 or the mean pulmonary artery pressure was greater than 30 mm Hg. Only emergency operation increased the risk of operative death in the group with isolated aortic valve replacement.

The multivariate stepwise logistic regression analysis identified emergency operation and increased age as the two significant determinants of risk, whereas pulmonary capillary wedge pressure, cardiac index, mean pulmonary artery pressure and combined aortic valve replacement and coronary artery bypass grafting had no independent predictive

Table 5. Valve-related Complications in 23 Cases

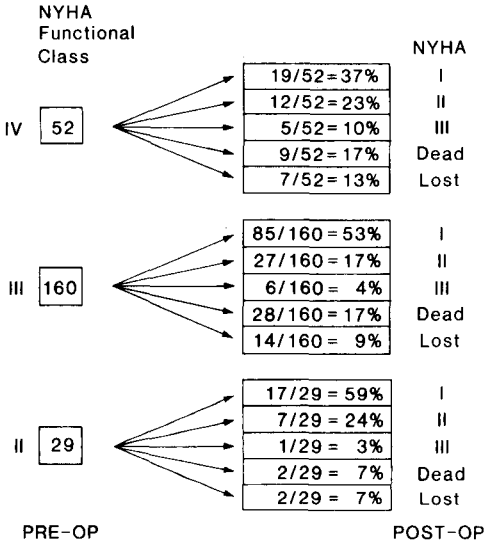
	Events	Percent per Patient-Year
Thromboembolism	3	0.29
Stroke	2	0.19
Bacterial endocarditis	2	0.19
Hemorrhage	7	0.69
Paravalvular leak	8	0.79
Tissue valve stenosis	1	0.20
Valve fracture	0	0.00

value. If only elective cases were considered, the analysis indicated that the preoperative cardiac index and functional class were the strongest determinants of operative mortality.

Late mortality. At a mean follow-up time of 48 months, 72% of the 241 patients who had survived their operation were still living and 10% were lost to follow-up. Late mortality rate within the aortic valve replacement group did not differ among those with aortic stenosis, aortic regurgitation or mixed stenosis and regurgitation. Late mortality rate for patients having the combined operation was higher, but they also had a higher mean preoperative age. Even though the risk of operative death was greater for patients undergoing emergency procedures, the late mortality rate for these patients was not significantly higher than for those who had an elective operation. The late mortality rate for patients older than 70 years was 23%.

Predictors of late mortality. Using the stepwise Cox regression analysis, a relative hazard function was developed. The elements that correlated with an increased late mortality rate were preoperative age, male sex, left ventricular end-diastolic pressure, functional class and cardiac index. Whether or not the operation was performed on an emergency basis had no effect on the late mortality rate.

Figure 2. Functional results for 241 operative survivors. NYHA = New York Heart Association; POST-OP = postoperative; PRE-OP = preoperative.



Complications. There were no significant differences between the need to reoperate on mechanical valves and bioprosthetic valves. The incidence rate of each valve-related complication such as thromboembolism, paravalvular leak, bacterial endocarditis or hemorrhage was less than 1% per patient-year (Table 5). The incidence of these complications in the mechanical and bioprosthetic valves was not significantly different.

Late functional results (Fig. 2). Overall, 77% of the long-term survivors were in functional class I or II at a mean follow-up time of 48 months. Significant improvement was noted in all groups of patients, including those in preoperative class IV. Of the 40 patients who survived emergency operation, 75% were in class I or II, 2% were in class III, 13% had died and 10% were lost for follow-up examination. Of the 44 operative survivors who were older than 70 years, 70% were in class I or II, 23% had died and 7% were lost to follow-up.

Discussion

Recent large clinical reviews (1–4) of aortic valve replacement and aortic valve replacement combined with coronary artery bypass grafting cover patients operated on between 1967 and 1981. These reports confirm that the operative mortality rate has fallen since the mid-1970s, despite an increase in the number of high risk patients undergoing elective operation (4). This has been attributed to the adoption of cardioplegia techniques for myocardial preservation and advances in pre- and postoperative care (3,4). With this fact in mind, we chose to analyze only patients undergoing operation between 1978 and 1984. Cardioplegia, induced with cold crystalloid cardioplegia solution and topical hypothermia, was used for myocardial protection in all patients. All angiographically significant coronary stenoses were bypassed and all patients were monitored in a modern intensive care unit for at least 24 hours postoperatively. This approach has allowed us to study which other factors might affect operative results, although it has shortened the period of long-term follow-up.

High risk groups for operative death. Multivariate analysis for determinants of operative death selected emergency operation and age greater than 70 years as the most significant risk factors. Most of the deaths in our series were attributed to these two conditions. Few investigators have reported the results of emergency aortic valve replacement. Wells et al. (5) published the results of 100 emergency cardiac operations with an operative mortality rate of 24%. These were all performed, however, in the era before cardioplegia (1973 to 1978) and included a variety of operations that ranged from emergency coronary artery bypass grafting to acute aortic dissection. Emergency valve replacement

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(aortic, mitral or both) carried a mortality rate of 22.4%. Several reports (6–8) dealing with valve replacement for bacterial endocarditis have appeared, with the operative mortality rate ranging from 9 to 31%. With respect to isolated aortic valve replacement, we have found that emergency operation is associated with an eightfold increase in mortality rate compared with that of elective operation. In our series the number of patients requiring emergency aortic valve replacement with coronary artery bypass grafting was small, but the operative mortality rate was 40%. Five of the six deaths in this group, however, occurred in patients older than 70 years.

Several studies (9–12) have demonstrated that valve replacement in patients over 70 years of age carries a higher operative mortality rate that ranges from 5 to 11% for elective operation. Only one study (11) included emergency aortic valve replacement in elderly patients, and in this group the operative mortality rate was high (40%). However, because only five cases were analyzed and several of these patients were operated on in an earlier era (1970 to 1976), no firm conclusions were drawn. In our experience, elective aortic valve replacement in the elderly increases the mortality rate to 5.8% and elective aortic valve replacement with coronary artery bypass grafting in the elderly raises the mortality rate to 14.3%. The major jump in deaths, however, occurs in patients who are older than 70 years and have an emergency operation; the mortality rate in this group increases to 31%. This is not unexpected, but it does point out the danger of delaying elective operation until the clinical state of elderly patients deteriorates.

Univariate analysis selected patients having combined aortic valve replacement and coronary artery bypass grafting as a high risk group, whereas multivariate analysis selected only emergency operation and age greater than 70 years as significant risk factors. Thus, patients having isolated aortic valve replacement and those having the combined operation are not comparable groups, because a higher proportion of elderly and emergency patients are in the combined group. In this study, therefore, the higher mortality rate for patients having the combined operation reflects the higher natural risk of this patient group, rather than any increased risk from the combined operation.

If only elective cases were analyzed, the overall operative mortality rate dropped to 1.5% for isolated aortic valve replacement and 8.1% for the combined operation. Multivariate analysis then selected factors indicative of impaired left ventricular function (cardiac index < 2.0 liters/min per m^2 and functional class IV) as the best predictors of operative death. This is consistent with findings of other studies (4). Again, the addition of coronary artery bypass grafting to aortic valve replacement had no independent effect on the mortality rate in elective operations.

If patients older than 70 years and emergency cases are omitted from the analysis, the operative mortality rate was quite low. Thus, elective aortic valve replacement in patients under 70 now carries an operative mortality rate of less than 1%. In our series, elective aortic valve replacement and coronary artery bypass grafting in patients under 70 carries an operative mortality rate of 5.7%.

Late results and complications. Our incidence of valve-related complications was low and comparable with that of other studies (1,3). We found no difference in the incidence of complications or valve failure between bioprosthetic and mechanical valves. There were no cases of catastrophic failure of any valve, including the 77 Björk-Shiley valves observed for 308 patient-years. In a mean follow-up time of 4 years, there was only one case of tissue valve stenosis.

Late functional results and late mortality in this series are similar to those of other reports (1–3). Factors found to affect long-term survival were preoperative age, male sex, left ventricular end-diastolic pressure, cardiac index and functional class. Although the late mortality in patients over 70 years was higher than for those under 70, it was not excessive. Seventy-seven percent of the elderly who survived operation are still living after 4 years. Moreover, all late survivors in this group were in functional class I or II. With the exception of male sex, the other factors that influence survival have also been shown by others to adversely affect survival. In general, they reflect advanced preoperative left ventricular dysfunction (1,3,13). Why men have a shorter survival than women is not clear.

Several factors had no effect on late results. We found no difference in late survival for patients with aortic stenosis, aortic regurgitation or mixed stenosis and regurgitation. Although patients having the combined operation had a higher late mortality rate, multivariate analysis did not show the combined operation to be an independent determinant. Thus, the poorer survival in this group can be accounted for by differences in age, sex and left ventricular function. Although early mortality was higher in patients having an emergency operation, this had little effect on late survival. Moreover, late functional results in this group were excellent.

Conclusions. With the improvements in myocardial preservation, operative techniques and preoperative and postoperative care, elective aortic valve replacement in patients under 70 years of age now carries an operative mortality rate of less than 1%. Most operative deaths occur in several easily recognized groups. Patients having emergency operation and those older than 70 are at high risk. Elderly patients having emergency operation are at the highest risk. In this series, patients having aortic valve replacement and coronary artery bypass grafting had a higher operative mortality rate, but this reflects the greater number of emergency, elderly and decompensated patients in this group, rather than an inherent risk in the combined operation. Combined aortic valve replacement and coronary artery bypass grafting is appropriate when aortic valve disease and significant coro-

nary artery stenoses coexist. Late functional results and survival are good for all groups of patients, even those who require emergency operation and those who are older than 70 years. With respect to all of the factors considered in this analysis, we do not recognize any contraindications to aortic valve replacement.

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